IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

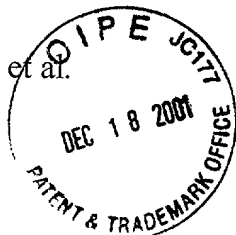In re Application of:

Garry Taylor et al.

Serial No.: 09/915,515 : Art Unit: 2671

Filed: July 27, 2001 : Examiner:

For: THREE DIMENSIONAL : Atty Docket: 21663/0193
STRUCTURE OF
PARAMYXOVIRUS :
HEMAGGLUTININ-
NEURAMINIDASES AND USE :
THEREOF

[Stamp: OIPE DEC 18 2001 PATENT & TRADEMARK OFFICE]

TRANSMITTAL OF SUBSTITUTE DRAWINGS

Commissioner for Patents
Washington, D.C. 20231

Sir:

As required by the Notice to File Missing Parts of Nonprovisional Application, attached are substitute drawings in compliance with 37 CFR 1.84. The drawings consist of 6 sheets comprising Figs. 1-5.

Respectfully submitted,

[Signature]

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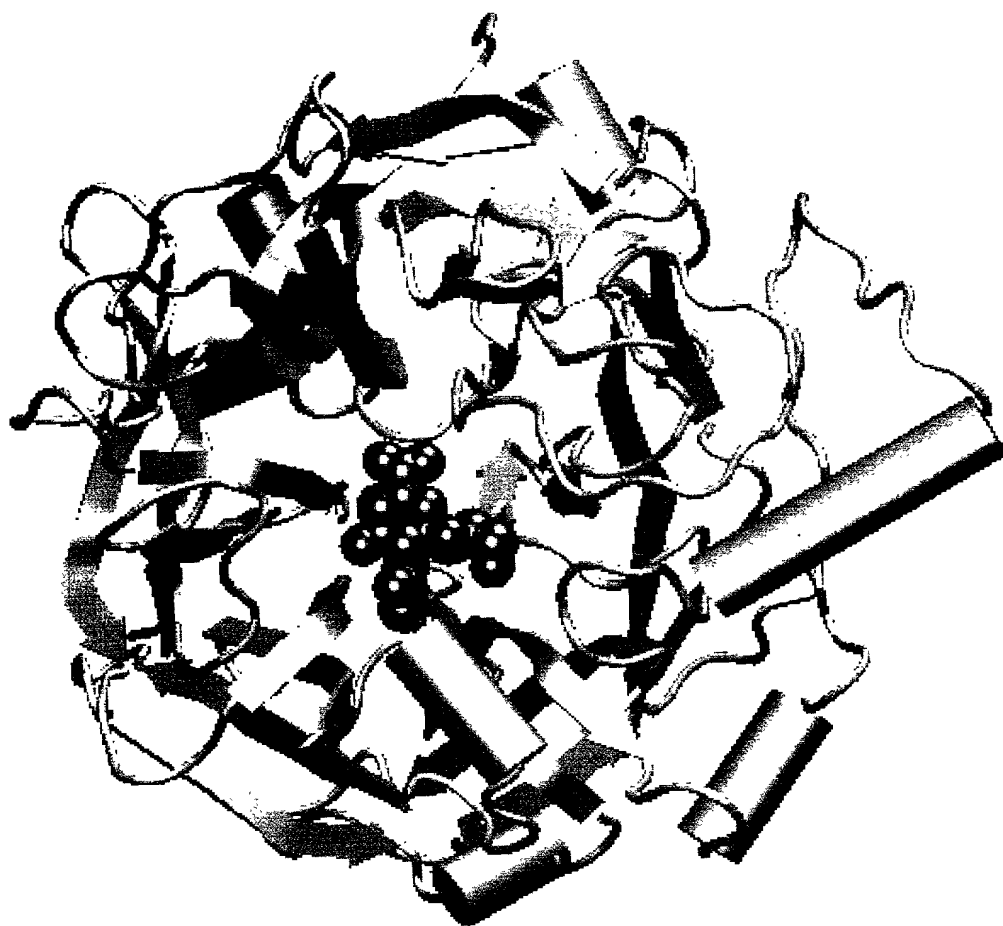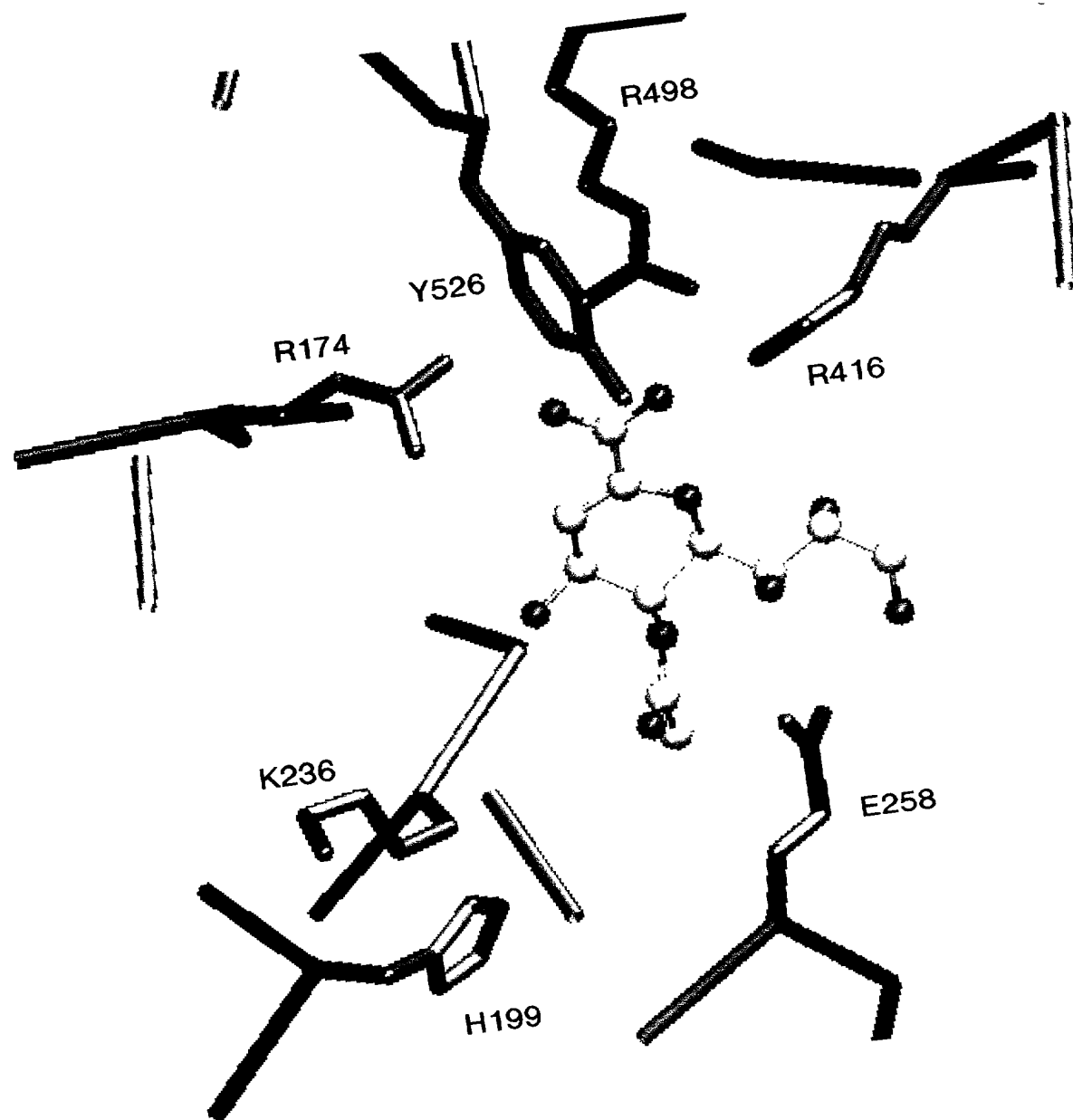
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FIG. 1

Protein sequence alignment (rotated 90° on page).

Block 1

```
Sendai        TIAVHHAEGIAPLEPHSFWRCPVGEPYLSSDPKISLLLGPSLLSGSTTISGCVRLPSLSIGEAIYAYSSNLITQGCADIGKSYQVLQLGYISLNSDMPP
PIV1          TIAIHHADGISPLPHDFWRCPVGEPYLSSDPKISLLLGPSLLSGSTTISGCVRLPSLSIGDAIYAYSSNLITRGCQDIGKSYQVLQLGIITVNSDLVP
PIV3          RIT..HDVGIKPLNPDDFWRCTEGLPSLMKTPKIRLMPGPGLLAMPTTVDGCVRTPSLVINDLIYAYTSNLITHNVILNGCQDHVSNQFVSMGIIEPTSAGFP
SV5           AALINDNRYINGINQFYFSIAEGRNLTL..GP...LLNMPSFIPTATTPEGCTRIPSFSLIKTHWCYTHNVILGDCLDFTTSNQYLAMGIIQQBAAAFP
PIV2          NLLEDAAYINGLNKFLVLKSYNGTPKY...GP...PLNMPSFIPTATSPNGCTRIPSFSLGKTHWCYTHNVINANCKDHTSSNQYISMGILVQTASGYP
Mumps         IPLVNDLRFINGINKFIIEDYATEDFSI..GH...PLNMPSFIPTATSPNGCTRIPSFDMSATHYCYTHNVILSGCRDHSHSHQYLALGVLRTTATGRI
NDV    (124)  GAPIHDPDFIGGIGKELIVDNASDVTSFYPSA...FQEHLNFIPAPTTGSGC
```

Secondary structure: β6S4 · β1S1 · β1S2 · β1S3

Block 2

```
Sendai        DLNPVVSHTYDINDNRKSCSVVATGTRGYQLCSMPTVDERTDYSSDGIEDLVLDLKGSTKSHRYRNSEVDLDHPFSALYPSVGNGIATEGSLIPLG
PIV1          DLKPVISHTYDINDNRKSCSVIAAGTRGYQLCSLPTVNETTDYSSEGIEDLVFDILDLKGTKSHRCKNEDITFDHPFSAMYPSAYPSVGPGIYYKGKIIFLG
PIV3          DLNPRISHTFNINDNRKSCSLALLNTDVYQLCSTPKVDERSDYASSGIEDIVLDIVNHDGSISTTRFKNNNISFDQPYAALYPSTGSGVYYLGWLFPI
SV5           FFRTLKTLYLSDGVNRKSCSISTVPGGCMMYCFVSTQPERDDYFSBAAPPEQRIIMYNDTIVERII..NPPGVLDVWATLNPAVGSGIYHLGFILPPV
PIV2          IFRTMKTIYLSDGINRKSCSIATPGGCYICYVATRSEKEDYATTDLAELRLAFYYYNDTFIERVI..SLPNTTGQWATINPAVGSGIYFENKLIFPA
Mumps         MFKTLKIQYLSDGLNRKSCSIATVPDGCAMYCYVSTQLETDDYAGSSPPTQKLTLLFYNDTVTERTI..DVTTLFEDWVANYPGVGGGSFIDGRVWFSV
NDV    (220)  FFSTLRSISLDDTQNRKSCSVSATPLGCDMLCSKVTETEBEDYNSAVPTLMAHGRLGFPDGQYHEKDL.
```

Secondary structure: β5S0 · β1S1 · β1S2 · β1S3 · β2S3 · β2S4 · α1 · α2 · β3S1a · β3S1b · β3S2

Block 3

```
Sendai        YGGLTTPLQGDTKCRT.........QGCQQVSQDTCNEALKI...TWLGGKQVVNVIIRVNDYLSERPKIRVTTIPITQNYLGAEGRLLKLGDRVYIYT
PIV1          YGGLTTPLQGDTKCVT.........NRCANVNQSVCNDALKI...TWLKKRQVVNVLIRINNYLSDRPKIVVETIPITQNYLGAEGRLLKLGGKKIYIYT
PIV3          YGGLEHPINENAICNT.........TGCPGKTQRDCNQABHS...PWFSDRRMVNSIIVVDKGLNSIPKLKVWTISMRQNYWGSEGRLLLGNKIYIYT
SV5           YGGVIKGTSLWNNQANKYPIPQNVAALCSQNQATQVQNAKSSYYSSWFGNRMIQSGILACPLRQDLTNECLVLPFSNDQVLMGAEGRLYVIDNNLYYYQ
PIV2          YGGLIKGTPSYNKQSRYFIPKPHPNITCAGKSSEQAAAARSSYVIRYHSNRLLQSAVLICPLSDMHTARCNLVMFNNSQVMMGAEGRVLLINNRLLYYQ
Mumps         YGGVLPNSSLGVKSAREFFRPVNPYNPCSGPQQDLDQRALRSYFPSYFSNRRRVQSAFLVCANNQILVTNCELVVPSNNQTLMGAEGRILTVGTSHFLYQ
NDV    (317)  YGGLKPNSPSDTVQEGKYVIYKRYNDTCPDEQDYQIRMAKSSYKPGRFGGKRIQQAILSIKVSTSLGEDPVLTVPPNTVTLMGAEGRILTVGTSHFLYQ
```

Secondary structure: β3S2 · β2S1 · β2S2 · α3 · α4 · β3S3 · β3S4 · β4S1 · β4S2 · β5S1 · β5S2 · β5S3

Block 4

```
Sendai        RSSGWHSQLQIGVLDV...SH..PLTINWTPHEALSRPGNKECNWYNTCPKECISGVYTDAYPLSPDAAN........VATVTLYANTSRVNPTIM
PIV1          RSSGWHSHLQIGSLDI...NN..PMTIKWAPHEVLSRPGNQDCNWYNRCPRECISGVYTDAYPLSPDAVN........VATTTLYANTSRVNPTIM
PIV3          RSTSWHSKLQLGIIDI...TDYSDIRIKWTWHNVLSRPGNNECPWGHSCPDGCITGVYTDAYPLNPTGSI....VSSVILDSQKTRVNPVIT
SV5           RSNSWWPMTMLYKVTITFTNGQPSAISAQNVPTQQVPRPGTGDCSATNRCPGCLTGVYADAMLLTNPSSTB..TFGSEATFTGSYLNTATQRINPTMY
PIV2          RSSSWWSASLFYRINTDFSKGIPPIIEAQWVPSYQVRPGVMPCNATSFCPANCITGVYADVWFLNDPEPTSQNALMPNYRFAGAFLRNESRTNPTFY
Mumps         RSTSWPYELLYEISFTFTNSGQSSVNMSWIPIYSFTRPGSGNCSGENVCPTACVSGVYLDPMPLTPYSHQS..GINRNFYFTGALLNSSTTRVNPTLX
NDV    (416)  RGSSYFSPALLYPNTV...SNKTATLHSPYTFNAFTRPGSIPCQASARCPNSCVTGVYTDPYPLIFYRNHTLRGV........FGTMLDSEQARLNPASA
```

Secondary structure: β4S3 · β4S4 · β6S1 · β6S2 · β5S2

Block 5

```
Sendai        YSNTTNIINMLRIKDVQLEVAYTTISSCITHFGKG..YCFHIIEINQKSLNTLQPMLFKTSIPKLCKAES
PIV1          YSNTSEIINMLRLKNVQLEAAYTTTS.CITHFGKG..YCFHIVEINQTSLNTLQPMLFKTSIPKICKITS
PIV3          YSTATERVNELAIRNKTLSAGYTTTS.CFRDTGSVMVCIYIIELSSLLGQFQIVPFFIRQVTLS
SV5           IANNTQISSQQFGSSGQEAAYGHTT.CFKNTGTQKIYCLIIIEMGSSLLGEFQIIPFLRELIP
PIV2          TASASALLNTTGFNNTNHKAAYTSST.CFQDTGDASVYCVYIMELASNIVGEFQILPVLTRLTIT
Mumps         VSALNNLKVLAPYGNQGLFASYTTTT.CFKVVKTNKTYCLSIAEISNTLFGEFRIVPLLVEILKNDGVREARSG
NDV    (505)  VFDSTSRSRITRVSSSTKAAYTTST.
```

Secondary structure: β5S4 · β6S3

FIG. 2

R498

Y526

R174

R416

K236

E258

H199

FIG. 3

R498

R174

R416

Y526

K236

E258

H199

FIG. 4

	Native 1	Native 2	Native 3	Native 4	NANA	DANA
Cell (Å)	73.3	72.3	71.7	72.0	71.6	137.5
	78.0	77.9	77.9	83.8	77.6	137.5
	202.6	199.2	198.2	201.5	197.2	116.6
Temp(K), pH	293, 7	100, 4.6	100, 4.6	293, 6	100K, 4.6	100K, 6.5
Resolution (Å)	3.0	2.0	2.5	3.0	2.5	2.8
# obs	172104	623166	420703	277932	210555	498619
# unique	20022	68217	38168	22207	29671	38673
Complete ness(%)	83	86	97	88	76	94
R_{merg}(%)	9.3	4.9	3.1	9.3	4.2	5.2
R-factor			0.222		.223	0.209
R_{free}			0.277		.291	0.235
# protein atoms			6914		6914	6896
# CHO, Ca,			89		116	111

FIG. 5

ligands

# waters	211	207	239
<B> A, B Å^2	25.36	32,44	44,44
<B> ligand Å^2		38,57	48,41

Table 1 Crystallographic data and refinement statistics.

Datasets Native2, Native3, NANA and DANA from frozen crystals were collected on beamlines X11 and BW7A at DESY, Hamburg. All other datasets were collected on in-house rotating anode and image plate or multiwire detector systems.

$\text{Rmerge} = \Sigma_{hkl}\, \Sigma_i\, |\Sigma\, I^i_{hkl} - <I_{hkl}>| \,/\, \Sigma_{hkl}\, \Sigma_i <I^i_{hkl}>$ where the sum i is over all separate measurements of the unique reflections hkl.

$\text{R-factor} = \Sigma_{hkl}\, ||F_{obs}| - |F_{calc}||\, /\, \Sigma_{hkl}\, |F_{obs}|$

R_{free}, as R-factor but summed over a 10% test set of reflections.